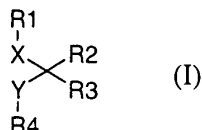


## CLAIMS

*Amn.*  
*a<sup>1</sup>*

1. A compound of general Formula I



5 or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R<sub>1</sub> represents,

C<sub>1</sub>-C<sub>6</sub> alkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

10 cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O,

15 and substituted with one or more basic groups such as amino, amidino and/or guanidino;

or aryl, substituted with one or more basic groups such as amino, amidino and/or guanidino,

R<sub>2</sub> represents H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl,

20 aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, Z<sub>2</sub>N-CO-O-, ZO-CO-NZ- or Z<sub>2</sub>N-CO-NZ- group,

R<sub>3</sub> represents COOR<sub>5</sub>, SO(OR<sub>5</sub>), SO<sub>3</sub>R<sub>5</sub>, P=O(OR<sub>5</sub>)<sub>2</sub>, B(OR<sub>5</sub>)<sub>2</sub>, P=OR<sub>5</sub>(OR<sub>5</sub>), or tetrazole, or any carboxylic acid isostere,

25 R<sub>4</sub> represents SH, S-CO-C<sub>1</sub>-C<sub>6</sub> alkyl or S-CO-aryl,

R<sub>5</sub> represents H, C<sub>1</sub>-C<sub>6</sub> alkyl or aryl,

R<sub>6</sub> represents H or C<sub>1</sub>-C<sub>6</sub> alkyl,

X represents O, S, SO, SO<sub>2</sub>, C(Z)<sub>2</sub>, N(Z), NR<sub>6</sub>SO<sub>2</sub>, SO<sub>2</sub>NR<sub>6</sub>, NR<sub>6</sub>CO or CONR<sub>6</sub>,

Y represents C(Z)<sub>2</sub>,

contd.  
a<sup>1</sup>

~~X represents independently H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, cycloalkyl or heterocyclyl.~~

~~2. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,~~

~~5 wherein~~

~~R<sub>1</sub> represents,~~

~~cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or~~

~~guanidino;~~

~~heterocyclyl, containing at least one nitrogen atom;~~

~~10~~

~~heterocyclyl, containing at least one hetero atom selected from S or O, and substituted~~

~~with one or more basic groups such as amino, amidino and/or guanidino;~~

~~or aryl, substituted with one or more basic groups such as amino, amidino and/or~~

~~guanidino;~~

~~R<sub>2</sub> represents H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl,~~

~~15~~

~~aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano,~~

~~cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, Z<sub>2</sub>N-~~

~~CO-O-, ZO-CO-NZ- or Z<sub>2</sub>N-CO-NZ- group,~~

~~R<sub>3</sub> represents COOR<sub>5</sub>,~~

~~R<sub>4</sub> represents SH, S-CO-C<sub>1</sub>-C<sub>6</sub> alkyl or S-CO-aryl,~~

~~20~~

~~R<sub>5</sub> represents H, C<sub>1</sub>-C<sub>6</sub> alkyl or aryl,~~

~~R<sub>6</sub> represents H or C<sub>1</sub>-C<sub>6</sub> alkyl,~~

~~X represents O, S, SO, SO<sub>2</sub>, C(Z)<sub>2</sub>, N(Z), NR<sub>6</sub>SO<sub>2</sub>, SO<sub>2</sub>NR<sub>6</sub>, or CONR<sub>6</sub>,~~

~~Y represents C(Z)<sub>2</sub>,~~

~~Z represents independently H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, cycloalkyl or heterocyclyl.~~

~~25~~

~~3. The compound according to claim 1 or 2, or a pharmaceutically acceptable salt or~~

~~solvate thereof, or a solvate of such a salt,~~

~~wherein~~

~~R<sub>1</sub> represents,~~

~~30~~

~~cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or~~

~~guanidino;~~

~~heterocyclyl, containing at least one nitrogen atom~~

contd.  
a<sup>1</sup>

heterocyclyl, containing at least one hetero atom selected from S or O, and substituted with one or more basic groups such as amino, amidino and/or guanidino;

R<sub>2</sub> represents H, C<sub>1</sub>-C<sub>3</sub> alkyl, amino, halogen, hydroxy,

R<sub>3</sub> represents COOR<sub>5</sub>,

5 R<sub>4</sub> represents SH, S-CO-C<sub>1</sub>-C<sub>6</sub> alkyl or S-CO-aryl,

R<sub>5</sub> represents H, C<sub>1</sub>-C<sub>6</sub> alkyl or aryl,

X represents C(Z)<sub>2</sub>,

Y represents C(Z)<sub>2</sub>,

Z represents independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

10

4. The compound according to any previous claim, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R<sub>1</sub> represents,

15 cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

R<sub>2</sub> represents H, F, or C<sub>1</sub> alkyl,

R<sub>3</sub> represents COOR<sub>5</sub>,

20 R<sub>4</sub> represents SH, S-CO-C<sub>1</sub>-C<sub>6</sub> alkyl or S-CO-aryl,

R<sub>5</sub> represents H, C<sub>1</sub>-C<sub>6</sub> alkyl or aryl,

X represents C(Z)<sub>2</sub>,

Y represents C(Z)<sub>2</sub>,

Z represents independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

25

5. The compound according to any previous claim, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R<sub>1</sub> represents cyclopentyl, pyridyl, pyrimidinyl, piperidinyl or thiazolyl,

R<sub>2</sub> represents H, F, or C<sub>1</sub> alkyl,

30 R<sub>3</sub> represents COOR<sub>5</sub>,

R<sub>4</sub> represents SH,

R<sub>5</sub> represents H,

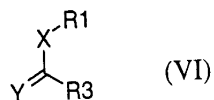
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Q1*

X represents CHZ,

Y represents CHZ,

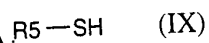
Z represents independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

- 5 6. A process for the preparation of a compound according to any one of claims 1-5, wherein R<sub>1</sub>, R<sub>3</sub>, R<sub>4</sub>, and Y are as defined in claim 1 and X is C(Z)<sub>2</sub> and R<sub>2</sub> is H, comprising the step of;  
reacting a compound of Formula VI,



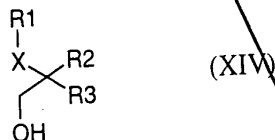
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wherein R<sub>1</sub>, R<sub>3</sub> and Y are as defined in claim 1 and X is C(Z)<sub>2</sub>, with a compound of Formula IX,

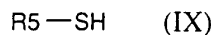


- 15 wherein R<sub>5</sub> is a suitable protecting group, such as Ac, Bz, PMB or Bn, alone or in the presence of a suitable base, such as NaOMe, NaH or triethylamine or alternatively in the presence of a free-radical initiator, such as AIBN under standard conditions.

7. A process for the preparation of a compound according to any one of claims 1-5, wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are as defined in claim 1 and Y is CH<sub>2</sub> and X is O, S, C(Z)<sub>2</sub>, or  
20 N(Z), comprising the step of:  
reacting a compound of Formula XIV,



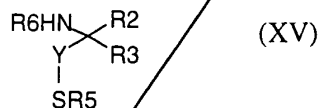
wherein  $R_1$ ,  $R_2$ , and  $R_3$  are as defined in claim 1 and X is O, S,  $C(Z)_2$ , or  $N(Z)$ , with a compound of general Formula IX,



wherein  $R_5$  is a suitable protecting group, such as Ac or Bz, in the presence of a suitable reagent, such as  $PPh_3$ /DIAD, under standard conditions.

8. A process for the preparation of a compound according to any one of claims 1-5, wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ , and Y are as defined in claim 1 and X is  $NR_6CO$ , or  $NR_6SO_2$  comprising the step of:

10 reacting a compound of the general Formula XV,



wherein  $R_2$ ,  $R_3$ ,  $R_6$  and Y are as defined in claim 1 and  $R_5$  is a suitable protecting group, such as Ac, Bz, PMB or Bn, with a compound of the general Formula XVI,



15 wherein  $R_1$  is as defined for in claim 1 and X is  $COOH$  or  $SO_2Cl$  in the presence of suitable coupling reagents, such as PyBOP/DIPEA, DCC/HOBt, EDC/TEA/DMAP or pyridine, under standard conditions.

20 9. A pharmaceutical formulation containing a compound according to any one of claims 1 to 5 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

*a*  
~~10. The use of a compound according to any one of claims 1 to 5 in therapy.~~

11. The use of a compound according to any one of claims 1 to 5 for the manufacture of a ~~medicament~~ for the inhibition of carboxypeptidase U.

Amem.  
Q2 5 12. A method for treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising administering to a mammal, including man, in need of such treatment an effective amount of a compound as defined in any of claims 1-5.

10 13. A pharmaceutical formulation for use in the treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising a compound as defined in any of claims 1-5 in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

14. A pharmaceutical formulation, comprising:

- 15 (i) a compound of Formula I or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, and
- (ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor ( $P_2T$ ) antagonist,
- 20 in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

15. A kit of parts comprising:

- (i) a pharmaceutical formulation containing a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
- 25 (ii) a pharmaceutical formulation containing one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor ( $P_2T$ ) antagonist,
- 30 in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

contd.  
a<sup>2</sup>

which compound (i) and agent (ii) are each provided in a form that is suitable for administration in conjunction with the other.

- 5 16. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a therapeutically effective total amount of
- (i) a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; in conjunction with
- 10 (ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P<sub>2</sub>T) antagonist,
- 15 in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

17. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a formulation as
- 20 defined in claim 14.

Add  
a<sup>3</sup>